10/560,823 final compound

Connecting via Winsock to STN

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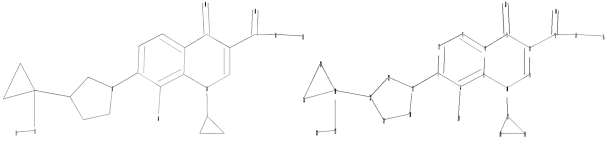
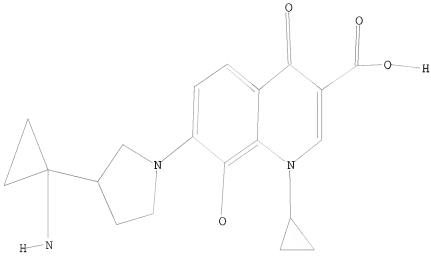


chain nodes :
12 13 14 15 16 27 28 29
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 17 18 19 20 21 22 23 24 25 26
chain bonds :
1-11 6-29 7-12 8-13 10-17 13-14 13-15 15-16 22-24 24-27 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-20 11-23 17-18 17-19
18-19 20-21 21-22 22-23 24-25 24-26 25-26
exact/norm bonds :
1-11 4-7 5-10 6-29 7-8 7-12 8-9 9-10 10-17 11-20 11-23 24-27
exact bonds :
8-13 15-16 17-18 17-19 18-19 20-21 21-22 22-23 22-24 24-25 24-26 25-26
27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-15
isolated ring systems :
containing 1 : 11 : 17 : 24 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom
19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:CLASS
28:CLASS 29:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

L2 19 SEA SSS FUL L1

=> file ca

=> s l2
L3 40 L2

=> d ibib abs fhitstr 1-40

L3 ANSWER 1 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:493695 CA
TITLE: Method for producing quinolonecarboxylic acid derivatives
INVENTOR(S): Sato, Koji; Sakuratani, Kenji
PATENT ASSIGNEE(S): Daiichi Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 32pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008126384	A1	20081023	WO 2008-JP817	20080331

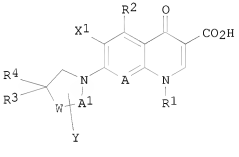
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2007-90650 A 20070330

OTHER SOURCE(S): CASREACT 149:493695; MARPAT 149:493695

GI



I

AB The title compds. I [A1 = (CH2)n; R1 = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted Ph, etc.; R2 = (un)substituted amino, H, alkyl, etc.; X1 = H, halo; A = N, CX2; X2 = H, cyano, halo, etc.; X2 and R1 and a part of the main nucleus may be united to form an (un)substituted ring; W = CHR5, O, NR6; R5 = H, halo, (un)substituted alkyl, etc.; R6 = H, alkyl, cycloalkyl; Y = H, alkyl, amino (connected to an optional C atom on the saturated hetero ring), etc.; n = 0 - 2; R3, R4 = H, halo, (amino-substituted) cycloalkyl, etc.; further details related to R3 and R4 are given] are prepared by reaction of a haloquinolonecarboxylic acid derivative with a cyclic amine salt and a boron derivative in a solvent in the presence of a base. I are antibacterials (no data). Thus, 1-cyclopropyl-1,4-dihydro-6-fluoro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid was prepared by reaction of 1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylic acid with 2-methylpiperazine dihydrochloride in acetonitrile containing triethylamine and BF3-THF complex.

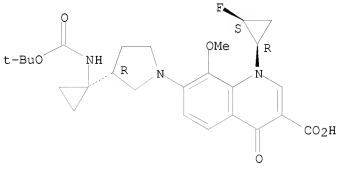
IT 817194-48-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of quinolonecarboxylic acid by reaction of haloquinolonecarboxylic acid with cyclic amine salt and boron compound in solvent in presence of base.)

RN 817194-48-2 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-[1-[[(1,1-dimethylethoxy)carbonyl]amino]cyclopropyl]-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:386639 CA
TITLE: Method for manufacturing quinolone compound-containing freeze-dried compositions
INVENTOR(S): Nishimoto, Norihiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 41pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

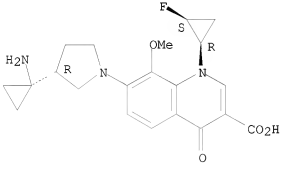
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2008231067	A	20081002	JP 2007-75875	20070323
PRIORITY APPLN. INFO.:			JP 2007-75875	20070323

OTHER SOURCE(S): MARPAT 149:386639

AB It is intended to provide a method for manufacturing a freeze-dried composition containing only a quinolone compound and a pH adjuster, which is excellent in resoly. Disclosed is a method for amorphous freeze-dried composition including (1) cooling a solution containing a quinolone compound with specified formula, e.g.
levofloxacin, ofloxacin, sitafloxacin, etc., and a pH adjuster for obtaining a frozen body, (2) increasing the temperature of the frozen body (especially, annealing at −20 - −2°), and (3) re-cooling thereof to give a freeze-dried product. For example, levofloxacin 8000 mg was dissolved in water 350 mL, and the pH was adjusted to 7 with HCl/NaOH solution The solution 10 mL was filled in a vial, and subjected to a freeze-dryer for (1) cooling at 0.15°/min to −30° for 3 h, (2) increasing the temperature at 0.5°/min to −5° for 2 h, (3) cooling at 1°/min to −40° for ≥ 2 h, (4) vacuuming to 20 Pa at 15° for ≥ 30 h, and (5) holding the product at 25°

1Pa for ≥ 6 h.
IT 431058-65-0
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method for manufacturing quinolone compound-containing freeze-dried compns.)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

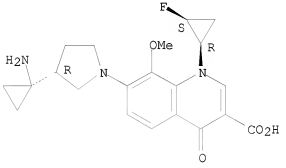
Absolute stereochemistry.



L3 ANSWER 3 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:298726 CA
TITLE: Physicochemical properties of antibacterial compounds: implications for drug discovery
AUTHOR(S): O'Shea, Rosemarie; Moser, Heinz E.
CORPORATE SOURCE: Achaogen Pharmaceuticals Inc., South San Francisco, CA, 94080, USA
SOURCE: Journal of Medicinal Chemistry (2008), 51(10), 2871-2878
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With the rise of multidrug-resistant pathogens and the need for novel antibiotics, it is critical to understand as much as possible from prior efforts and to apply learned lessons to the discovery of future antibiotics. One important parameter in particular has previously been mentioned but, in the view, not sufficiently analyzed: the physicochem. property space of antibacterial drugs. The authors selected 147 antibacterially active compds. that encompass both currently used drugs and compds. that are still under clin. investigation (see Methods for details). Where available, other property values were extracted from the literature, including protein binding and oral bioavailability in humans. This anal. suggests that natural products should be increasingly investigated again to identify novel antibacterial hits. Besides their high level of structural diversity, they are likely to better cover the required physicochem. property space for antibacterial compds. compared to synthetic mols. because of an increased d. of polar functionalities.
IT 431058-65-0, DX-619

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (physicochem. properties of antibacterial compds. and implications for drug discovery)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:533156 CA
TITLE: In Vitro antibacterial activity of DX-619, a novel Des-F (6)-quinolone against clinical isolates in china
AUTHOR(S): Xiao, Yonghong; Li, Yun; Liu, Jian; Zhong, Wei; Yang, Weiwei
CORPORATE SOURCE: Institute of Clinical Pharmacology, First Hospital Peking University, Beijing, 100083, Peop. Rep. China
SOURCE: Journal of Chemotherapy (Firenze, Italy) (2007), 19(6), 632-642
CODEN: JCHEEU; ISSN: 1120-009X
PUBLISHER: E.S.I.F.T. srl
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the study was to investigate in vitro antibacterial activity and bactericidal effect of DX-619 and other nine comparators against 1,101 recently collected clin. bacterial isolates in China. The min. inhibitory concns. (MICs) of antimicrobials were determined by a CLSI recommended standard agar dilution method and the min. bactericidal concns. (MBCs) were examined by the broth dilution method. Time-kill curves against representative isolates of Staphylococcus aureus, enterococci, and Klebsiellia pneumoniae were also conducted. DX-619 exhibited excellent antibacterial activity against 1,101 clin. isolates, especially to multi-drug resistant Gram-pos. cocci. The MIC90s of DX-619 were ≤0.016 and 0.125 mg/L against methicillin-sensitive and -resistant S. aureus, 0.062 and 0.125 mg/L against methicillin-sensitive and -resistant S. epidermidis, resp., which were 8-512 and 64-128 fold lower than those of comparative fluoroquinolones. The MIC90s of DX-619 for penicillin-sensitive and -non-sensitive Streptococcus pneumoniae, Enterococcus faecalis and

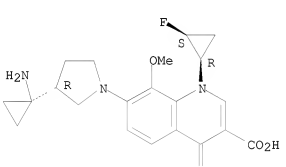
Enterococcus faecium were 0.016, 0.062, 0.25 and 0.5 mg/L, resp. The MIC90s of DX-619 against Enterobacteriaceae (except for Escherichia coli) and glucose-nonfermenting bacilli were ≤4 mg/L, which were comparable to other comparators. MBCs and time-kill curves showed that DX-619 was a potent bactericidal agent. There was no significant inoculum effect on MICs. But the activities of DX-619 against S. aureus, K. pneumoniae and Pseudomonas aeruginosa were decreased by acidic pH and human serum. DX-619 was a potent antibacterial compound against multi-drug resistant bacteria including Gram-pos. cocci, such as S. aureus and enterococci, which may warrant further exploration.

IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in Vitro antibacterial activity of DX-619 against clin. isolates in china)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:417108 CA
TITLE: Coagulase-negative staphylococcus infections - antibacterial therapy, therapeutic problems, and novel antibacterial agents
AUTHOR(S): Stock, Ingo
CORPORATE SOURCE: Bruehl bei Koeln, D-50321, Germany
SOURCE: Chemotherapie Journal (2008), 17(1), 10-24
CODEN: CHJOFT; ISSN: 0940-6735
PUBLISHER: Wissenschaftliche Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German

AB A review. Several coagulase-neg. staphylococcus species are frequent agents of a variety of nosocomial and community-acquired infections, in particular in young children, infants, and in the elderly population. They are the leading agents of nosocomial sepsis in neonates and frequent causes of other blood-stream infections. Endocarditis and meningitis as well as various infections of the urinary tract, soft tissue, wound, eye,

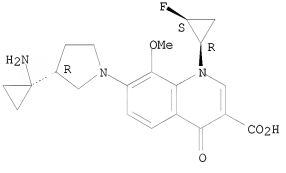
and skin are also attributed to these bacteria. The most frequent pathogen of many of these infections is Staphlococcus epidermidis, followed by S. hominis, S. haemolyticus, S. warneri, S. lugdunensis, and S. saprophyticus. Problems concerning the antibacterial treatment of staphylococcus infections arise from strains that have acquired resistances to several agents of different antimicrobial sub-groups, i.e., beta-lactams, aminoglycosides, fluoroquinolones, macrolides, lincosamides, fusidic acid, co-trimoxazole, and other antistaphylococcal agents. Another problem are biofilms that are frequently generated by the bacteria during indwelling medical device associated infections. Bacteria found in biofilms are often poorly controlled by current antistaphylococcal agents. Therefore, novel antibacterial substances with an enhanced activity against multiresistant strains as well as biofilm forming bacteria are strongly required. The currently most promising candidates for the treatment of infections due to coagulase-neg. staphylococci comprise linezolid, tigecycline and ceftobiprole as well as some new glycopeptides, i.e., dalbavancin, oritavancin, and telavancin. Iclaprim, the topical pleuromutilin retapamulin, the quinolone derivate DX-619 and the peptide deformylase inhibitor LBM415 might also represent attractive therapeutic agents and should be considered for further investigation.

IT 431058-65-0, DX-619
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibacterial therapy, therapeutic problems, and novel antibacterial agents for coagulase-neg. staphylococcus infections)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:73924 CA
TITLE: Susceptibilities of healthcare- and community-associated methicillin-resistant staphylococci to the novel des-F(6)-quinolone DX-619
AUTHOR(S): Watanabe, Shinya; Ito, Teruyo; Hiramatsu, Keiichi
CORPORATE SOURCE: Department of Infection Control Science, Graduate

	School of Medicine, Juntendo University, Hongo, Bunkyo-ku, Tokyo, 2-1-1, Japan
SOURCE:	Journal of Antimicrobial Chemotherapy (2007), 60(6), 1384-1387 CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER:	Oxford University Press
DOCUMENT TYPE:	Journal
LANGUAGE:	English

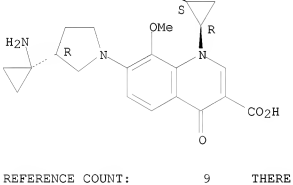
AB The activity of the novel des-F(6)-quinolone DX-619 against methicillin-resistant Staphylococcus was tested and compared with comparator antibiotics. MICs were determined by agar dilution method. The quinolone resistance regions of gyrA, gyrB, grlA, and grlB genes with reduced susceptibility to DX-619 were sequenced. DX-619 was point against all MRS tested and would be a promising candidate for the treatment of methicillin-resistant S. aureus infections.

IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoroquinolone DX-619 antibiotic activity against methicillin-resistant Staphylococcus aureus)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:	9	THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 40 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	147:330041 CA
TITLE:	Application of annealing to amorphous lyophilized drug product. (2). Establishment of annealing condition and scale-up method for production scale
AUTHOR(S):	Nishimoto, Norihiro; Takeuchi, Masahito; Abe, Masahiko
CORPORATE SOURCE:	Pharm. Technol. Res. Lab., Daiichi Pharmaceutical Co., Ltd., Takatsuki, 569-0806, Japan
SOURCE:	Material Technology (Tokyo, Japan) (2007), 25(3), 99-108 CODEN: MTECFQ
PUBLISHER:	Zairyo Gijutsu Kenkyu Kyokai
DOCUMENT TYPE:	Journal

LANGUAGE: Japanese

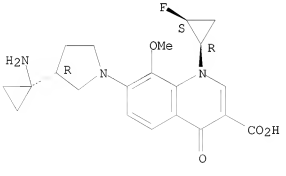
AB The objective of this study was to examine the effect of annealing condition on the reconstitution time for lyophilized drug products, and to develop set-up method and scale-up method of annealing condition. DX-619 drug substance was newly synthesized at Daiichi Pharmaceutical Co., Ltd. Annealing exceeding Tg' of DX-619 drug solution, the glass transition temperature of maximally freeze-concentrated amorphous phase, decreased the reconstitution time of DX-619 lyophilized drug product. The temperature profile of DX-619 frozen drug solution during annealing and the reconstitution time of DX-619 lyophilized drug product prepared by various annealing condition were measured in order to investigate the effect of annealing condition on the reconstitution time. In addition, the equation which correlates the temperature profile of frozen drug solution during annealing with the reconstitution time of lyophilized drug product was proposed to develop set-up method and scale-up method of annealing condition. The higher annealing temperature could reduce the annealing time to decrease of the reconstitution time of DX-619 lyophilized drug product. However, the effect of annealing on the reconstitution time of DX-619 lyophilized drug product was limited; reconstitution time reached plateau after a certain time of annealing. On the other hand, the annealing condition for DX-619 lyophilized drug product was fixed at -5° of shelf temperature for 30 min and at -10° of shelf temperature for 180 min using the proposed equation. Moreover, scale-up method of annealing condition with the proposed equation was developed considering the temperature distribution throughout the payload of lyophilizer. Regarding the lyophilized drug product located on the center of the middle shelf in the lyophilizer as the representative position, where the least effect of annealing on the reconstitution time of lyophilized drug product in the maximum payload was expected, made it possible to fix the annealing condition properly for the maximum payload of the lyophilizer.

IT 431058-65-0, DX-619
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(effect of annealing condition on reconstitution time of DX-619 lyophilized drug product)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



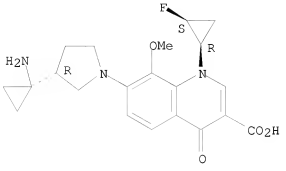
L3 ANSWER 8 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:158002 CA
TITLE: Lack of effect of DX-619, a novel des-fluoro(6)-quinolone, on glomerular filtration rate measured by serum clearance of cold iohexol
AUTHOR(S): Sarapa, Nenad; Wickremasingha, Prachi; Ge, NanXiang; Weitzman, Richard; Fuellhart, Merynda; Yen, Cindy; Lloyd-Parks, Julia
CORPORATE SOURCE: Daiichi Sankyo Pharma Development, Edison, NJ, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(6), 1912-1917
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB DX-619 is a novel des-fluoro(6)-quinolone with activity against a broad range of bacterial strains, including methicillin-resistant Staphylococcus aureus. The effects of DX-619 on the glomerular filtration rate (GFR) were evaluated because drug-related increases in serum creatinine levels were observed in studies with healthy volunteers. Forty-one healthy subjects were randomized to receive i.v. DX-619 at 800 mg or placebo once daily for 4 days, and the GFR was directly measured by determination of the clearance of a bolus iohexol injection in 33 subjects who completed the study per protocol. DX-619 was non-inferior to placebo for the GFR on the basis of a criterion for a clin. significant difference of -12 mL/min/1.73 m2. The mean GFRs on day 4 were 101.1±14.2 mL/min/1.73 m2 and 100.2±15.6 mL/min/1.73 m2 for the volunteers receiving placebo and DX-619, resp. On day 4 the mean serum creatinine concentration for volunteers receiving DX-619 increased by 30 to 40%, with a corresponding decrease in mean creatinine clearance. Both parameters normalized within 7 days after the cessation of DX-619 treatment. Non-clin. studies suggest that DX-619 increases the serum creatinine concentration by inhibiting excretory tubular transporters. In conclusion, DX-619 administered i.v. at 800 mg once a day for 4 days did not affect the GFR in healthy volunteers. Glomerular toxicity is not expected to present a risk to patients receiving DX-619 in clin. trials, but monitoring of the renal function, with an emphasis on the serum creatinine concentration, is still warranted.

IT 431058-65-0, DX-619
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lack of effect of DX-619 on glomerular filtration rate measured by serum clearance of cold iohexol)

RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

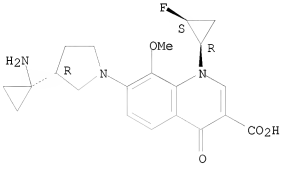
L3 ANSWER 9 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:487244 CA
TITLE: Application of annealing to amorphous lyophilized drug product. (1). Effect on the reconstitution time
AUTHOR(S): Nishimoto, Norihiro; Takeuchi, Masahito; Abe, Masahiko
CORPORATE SOURCE: Pharm. Technol. Res. Lab., Daiichi Pharmaceutical Co., Ltd., Takatsuki, 569-0806, Japan
SOURCE: Material Technology (Tokyo, Japan) (2007), 25(2), 74-82
CODEN: MTECFQ
PUBLISHER: Zairyo Gijutsu Kenkyu Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The objective of this study was to examine the effect of freezing condition on the reconstitution time for lyophilized drug products after lyophilization. Newly synthesized DX-619 lyophilized drug product was formulated with DX-619 drug substance and pH adjustments and did not contain any bulking agents. Although it took a long time, approx. 4 min, to reconstitute the DX-619 lyophilized drug products prepared by normal freezing condition, addition of an annealing exceeding the glass transition temperature of maximally freeze-concentrated amorphous phase of DX-619 drug solution (-15.2°) to the lyophilization cycle decreased the reconstitution time to approx. 20 s. Also, the DX-619 lyophilized drug product were characterized by SEM and x-ray powder diffraction to investigate the effect of the freezing condition. Whether annealing was added to the lyophilization cycle or not, the lyophilized drug product was not in a crystalline state but in an amorphous state. During annealing, however, ice crystal growth altered the shape of freeze-concentrate of DX-619 drug solution to change the morphol. of DX-619 lyophilized drug product after lyophilization. We presumed that the morphol. change of DX-619 lyophilized drug product increased the water penetration rate to decrease the reconstitution time.

IT 431058-65-0, DX-619
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(effect of annealing on reconstitution time in amorphous lyophilized drug, DX-619)

RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.

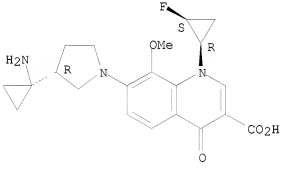


L3 ANSWER 10 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:387110 CA
TITLE: Method for production of quinolone-containing lyophilized preparation
INVENTOR(S): Nishimoto, Norihiro
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007037330	A1	20070405	WO 2006-JP319307	20060928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1930006	A1	20080611	EP 2006-810754	20060928
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
US 20080300403	A1	20081204	US 2008-67826	20080324
PRIORITY APPLN. INFO.:			JP 2005-282393 A	20050928
			WO 2006-JP319307 W	20060928

OTHER SOURCE(S): MARPAT 146:387110
AB Disclosed is a lyophilized preparation which contains only a quinolone-type synthetic anti-bacterial compound and a pH adjusting agent and has an excellent re-solubilizing property. Also disclosed is a method for production of a lyophilized preparation comprising a quinolone-type synthetic anti-bacterial compound as an active ingredient. The method comprises the steps of cooling an aqueous solution containing a quinolone-type synthetic anti-bacterial compound and a pH adjusting agent to yield a frozen material, increasing the temperature temporarily, and re-cooling the material to lyophilize the material.
IT 431058-65-0P
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(manufacture of lyophilized prepns. containing quinolone-type antibacterials)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

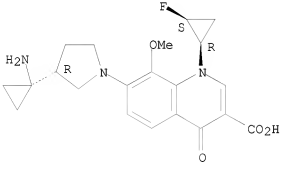
L3 ANSWER 11 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:375675 CA
TITLE: Antistaphylococcal activity of DX-619 alone and in combination with vancomycin, teicoplanin, and linezolid assessed by time-kill synergy testing
AUTHOR(S): Credito, Kim; Lin, Genrong; Appelbaum, Peter C.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(4), 1508-1511
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Time-kill synergy studies testing in vitro activity of DX-619 alone and with added vancomycin, teicoplanin, or linezolid against 101 Staphylococcus aureus strains showed synergy between DX-619 and

teicoplanin at 12 to 24 h in 72 strains and between DX-619 and vancomycin in 28 strains. No synergy was found with linezolid, and no antagonism was observed with any combination.

IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DX-619 alone and combined with vancomycin, teicoplanin, and linezolid antibiotic activity against Staphylococcus aureus assessed by time-kill synergy testing)

RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

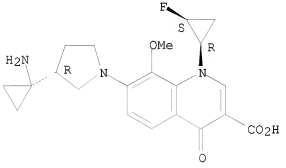
L3 ANSWER 12 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:201949 CA
TITLE: Activity of DX-619 compared to other agents against viridans group streptococci, Streptococcus bovis, and Cardiobacterium hominis
AUTHOR(S): Kosowska-Shick, Klaudia; Smith, Kathy; Bogdanovich, Tatiana; Ednie, Lois M.; Jones, Ronald N.; Appelbaum, Peter C.
CORPORATE SOURCE: Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(12), 4191-4194
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Against 198 viridans group streptococci, 25 Streptococcus bovis strains, and 5 Cardiobacterium hominis strains, MICs of DX-619, a des-F(6)-quinolone, were between 0.004 and 0.25 μg/mL. These MICs were lower than those of other quinolones (≤0.008 to > 32 μg/mL). β-Lactam MICs were between ≤0.008 and 16 μg/mL. Azithromycin resistance was found in most species, while most were telithromycin susceptible. Glycopeptides and linezolid were active against viridans group strains but inactive against C. hominis.

IT 431058-65-0, DX-619

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic activity of DX-619 and quinolone resistance in Streptococcus)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:138693 CA
TITLE: Molecular characteristics and in vitro susceptibility to antimicrobial agents, including the des-fluoro(6) quinolone DX-619, of Panton-Valentine leucocidin-positive methicillin-resistant Staphylococcus aureus isolates from the community and hospitals
AUTHOR(S): Yamamoto, Tatsuo; Dohmae, Soshi; Saito, Kohei; Otsuka, Taketo; Takano, Tomomi; Chiba, Megumi; Fujikawa, Katsuko; Tanaka, Mayumi
CORPORATE SOURCE: Division of Bacteriology, Department of Infectious Disease Control and International Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(12), 4077-4086
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Highly virulent, community-acquired methicillin-resistant Staphylococcus aureus (MRSA) strains with Panton-Valentine leucocidin (PVL) genes have been found increasingly worldwide. Among a total of 2101 MRSA strains isolated from patients in hospitals in Japan, two were pos. for PVL genes. One strain was identified as a community-acquired MRSA strain with genotype sequence type 30 (ST30) and spa (staphylococcal protein A gene) type 19 from Japan and was resistant only to β-lactam antimicrobial agents. The other strain was closely related to PVL+ multidrug-resistant,

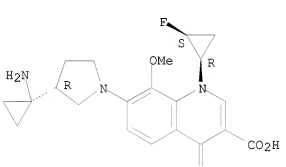
hospital-acquired MRSA strains (ST30, spa type 43) derived from nosocomial outbreaks in the 1980s to 1990s in Japan but with a divergent sequence type, ST765 (a single-locus variant of ST30). Twenty-two PVL+ MRSA strains, including those from Japan and those from other countries with various sequence types (ST1, ST8, ST30, ST59, and ST80) and genotypes, were examined for susceptibility to 31 antimicrobial agents. Among the agents, DX-619, a des-fluoro(6) quinolone, showed the greatest activity, followed by rifampin and sitafloxacin, a fluoroquinolone. The data suggest that DX-619 exhibits a superior activity against PVL+ MRSA strains with various virulence genetic traits from the community as well as from hospitals.

IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro susceptibility to antimicrobial agents of leucocidin-pos., methicillin-resistant Staphylococcus aureus isolates)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 40 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 146:117958 CA

TITLE: In vitro development of resistance to DX-619 and other quinolones in enterococci

AUTHOR(S): Wickman, Paul A.; Black, Jennifer A.; Smith Moland, Ellen; Thomson, Kenneth S.; Hanson, Nancy D.

CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Center for Research in Anti-Infectives and Biotechnology, Creighton University School of Medicine, Omaha, NE, 68178, USA

SOURCE: Journal of Antimicrobial Chemotherapy (2006), 58(6), 1268-1273
CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To investigate the mol. events involved in the development of quinolone resistance in enterococci. Clin. isolates of Enterococcus faecium and

Enterococcus fecalis were exposed to inhibitory and subinhibitory concns. of DX-619, ciprofloxacin, levofloxacin, gatifloxacin, and moxifloxacin. Mutational frequencies were calculated and susceptibility changes were determined

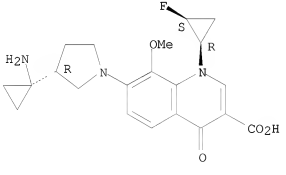
The quinolone resistance determining regions (QRDRs) of gyrA and parC in less-susceptible mutants were amplified by PCR and sequenced. Single-step mutants of E. fecalis and E. faecium were selected with all drugs. There were no differences in the frequencies of mutant selection among drugs, with frequencies ranging from 10-5 to 10-8. All single-step mutants were inhibited by 0.03-1 mg/L DX-619, 0.25-8 mg/L moxifloxacin, 0.5-8 mg/L gatifloxacin, 1-16 mg/L levofloxacin and 1-32 mg/L ciprofloxacin. No QRDR changes were observed in single-step mutants. Less-susceptible mutants selected after five passages on agar containing subinhibitory quinolone concns. were inhibited by 0.12-8 mg/L DX-619, 1-64 mg/L moxifloxacin, 2-64 mg/L gatifloxacin and 2-128 mg/L levofloxacin and ciprofloxacin. QRDR changes were detected in only 9 of the 20 fifth-passage mutants, suggesting that mutations outside the purported QRDRs and/or other resistance mechanisms were also involved. The relatively high frequencies at which single-step mutants were selected with all drugs indicate that caution is necessary if quinolones are to be considered for monotherapy of serious enterococcal infections. DX-619, the most potent quinolone, may have potential as an anti-enterococcal agent if sufficient concns. can be safely attained in vivo.

IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinolone resistance in Enterococcus)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:114330 CA
TITLE: Interactions of fluoroquinolone antibacterials, DX-619 and levofloxacin, with creatinine transport by renal organic cation transporter hOCT2
AUTHOR(S): Okuda, Masahiro; Kimura, Naoko; Inui, Ken-ichi

CORPORATE SOURCE: Department of Pharmacy, Kyoto University Hospital, Faculty of Medicine, Kyoto University, Kyoto, Japan
SOURCE: Drug Metabolism and Pharmacokinetics (2006), 21(5), 432-436
CODEN: DMPRB8; ISSN: 1347-4367
PUBLISHER: Japanese Society for the Study of Xenobiotics
DOCUMENT TYPE: Journal
LANGUAGE: English

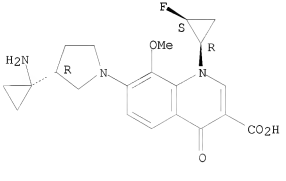
AB Interactions of DX-619, a novel fluoroquinolone antibacterial, and levofloxacin (LVFX) with the human renal organic cation transporter hOCT2 were studied. The intracellular accumulation of [14C]creatinine in stable transfectants of HEK293 cells expressing hOCT2 (hOCT2-HEK293) as well as vector-transfected HEK293 cells (VEC-HEK293) was evaluated in the presence of DX-619 and LVFX at various concns. When added extracellularly, both DX-619 and LVFX inhibited the uptake of [14C]creatinine (5 μM) by hOCT2-HEK293 cells in a dose-dependent manner. Unlike in hOCT2-HEK293 cells, the uptake in VEC-HEK293 cells was not inhibited by either fluoroquinolone suggesting that hOCT2 was specifically involved in the inhibition. The apparent IC50 value for the inhibition of [14C]creatinine uptake in hOCT2-HEK293 cells was 1.29 ± 0.23 μM for DX-619 and 127 ± 27 μM for LVFX, indicating DX-619 to be .apprx. 100-fold more potent than LVFX at inhibiting the transport of [14C]creatinine by hOCT2. A Dixon plot revealed that the inhibition by DX-619 of the hOCT2-mediated transport of [14C]creatinine was competitive. Fluoroquinolone antibacterials have the ability to inhibit the transport of creatinine by hOCT2, with DX-619 being much more effective than LVFX.

IT 431058-65-0, DX-619
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoroquinolone antibacterials DX-619 and levofloxacin interaction with creatinine transport by renal organic cation transporter hOCT2)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.

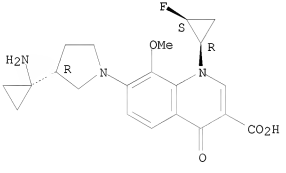


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 40 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 145:434616 CA
TITLE: In vitro antianaerobic activity of DX-619, a new des-fluoro(6) quinolone
AUTHOR(S): Tanaka, Kaori; Mikamo, Hiroshige; Nakao, Ken'ichi; Watanabe, Kunitomo
CORPORATE SOURCE: Division of Anaerobe Research, Life Science Research Center, Gifu University, 1-1 Yanagido, Gifu, 501-1194, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(11), 3908-3913
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vitro activity of DX-619, a new des-F(6) quinolone, against anaerobic bacteria was evaluated. DX-619 showed potent activity against Bacteroides, Prevotella, Fusobacterium, Micromonas, Actinomyces, and Clostridium spp., with MIC50s/MIC90s of ≤0.03 to 0.25/≤0.03 to 1 μg/mL, resp. DX-619 was also active against imipenem-resistant Bacteroides spp., with MIC50s/MIC90s of 0.25/1 μg/mL, resp.
IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antibiotic activity of quinolone DX-619 against anaerobic bacteria)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.

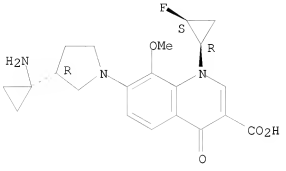


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:305758 CA
TITLE: Potency of DX-619, a novel des-F(6)-quinolone, in hematogenous murine bronchopneumonia caused by methicillin-resistant and vancomycin-intermediate Staphylococcus aureus
AUTHOR(S): Yanagihara, Katsunori; Seki, Masafumi; Izumikawa, Koichi; Higashiyama, Yasuhito; Miyazaki, Yoshitsugu;

Hirakata, Yoichi; Tomono, Kazunori; Mizuta, Yohei; Tsukamoto, Kazuhiro; Kohno, Shigeru
CORPORATE SOURCE: Second Department of Internal Medicine, Nagasaki University Graduate School of Pharmaceutical Sciences, Nagasaki University Graduate School of Medical Sciences, Nagasaki, 852-8501, Japan
SOURCE: International Journal of Antimicrobial Agents (2006), 28(3), 212-216
CODEN: IAAGEA; ISSN: 0924-8579
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, the potency of DX-619, a novel des-fluoro(6)-quinolone agent, was compared with that of vancomycin (VCM) in a murine model of hematogenous bronchopneumonia infection caused by methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-intermediate S. aureus (VISA). The min. inhibitory concns. (MICs) of DX-619 and VCM against MRSA were 0.03 μg/mL and 1.0 μg/mL, resp., while the MICs against VISA were 0.125 μg/mL and 8.0 μg/mL, resp. Treatment with DX-619 resulted in a significant decrease in the number of viable bacteria in the MRSA infection model (mean ± standard error of the mean for control, VCM and DX-619 groups: 7.97±0.32, 7.19±0.33 and 2.91±0.60 log10 colony-forming units/lung, resp.). For infection with VISA, mice were pre-treated with cyclophosphamide. The survival rate of mice treated with DX-619 (90% survival) was significantly higher than survival rates in the other two groups (45% both for VCM and control groups; $P < 0.05$). Histopathol. examination revealed that inflammatory changes in the DX-619-treated group were less marked than in the other two groups. The parameters in lung tissue for the area under the concentration-time curve/MIC ratio both for MRSA and VISA were higher in the DX-619 group than in the VCM group. Our results emphasize the potency of DX-619 against MRSA and VISA murine hematogenous pulmonary infection.
IT 431058-65-0, DX 619
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potency of DX-619 in hematogenous murine bronchopneumonia caused by methicillin-resistant and vancomycin-intermediate Staphylococcus aureus)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:284182 CA
TITLE: Intracellular penetration and activity of DX-619 in human polymorphonuclear leukocytes
AUTHOR(S): Garcia, Isabel; Ballesta, Sofia; Murillo, Concepcion; Perea, Evelio J.; Pascual, Alvaro
CORPORATE SOURCE: Dept. of Microbiology, School of Medicine, University of Seville, Seville, Spain
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(9), 3173-3174
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

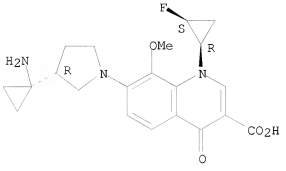
AB The intracellular penetration and activity of DX-619 in human polymorphonuclear leukocytes have been evaluated. DX-619 reached intracellular concns. 10 times higher than the extracellular concns. reached. Uptake was rapid, reversible, nonsaturable, and affected by environmental temperature, some metabolic inhibitors, and a soluble membrane activator. DX-619 showed intracellular activity against Staphylococcus aureus.

IT 431058-65-0, DX 619
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DX 619; intracellular penetration and activity of DX-619 in human polymorphonuclear leukocytes)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

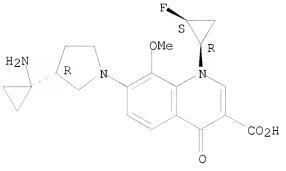
Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:4076 CA
TITLE: In vitro activities of DX-619 and comparison quinolones against Gram-positive cocci
AUTHOR(S): Wickman, Paul A.; Black, Jennifer A.; Moland, Ellen Smith; Thomson, Kenneth S.
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Center for Research in Anti-Infectives and Biotechnology, Creighton University School of Medicine, Omaha, NE, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(6), 2255-2257
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vitro activity of the novel quinolone DX-619 was compared to those of currently available quinolones against U.S. clin. isolates of Staphylococcus aureus, coagulase-neg. staphylococci, Enterococcus spp., Streptococcus pyogenes, and Streptococcus pneumoniae. DX-619 was the most potent quinolone overall, indicating possible utility as an anti-gram-pos. quinolone.
IT 431058-65-0, DX 619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antibiotic activity of DX-619 and quinolones against gram-pos. cocci)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

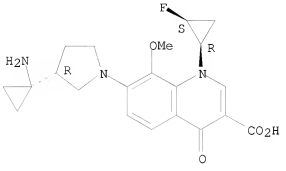
Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:428764 CA
TITLE: In vitro activities of DX-619 and four comparator agents against 376 anaerobic bacterial isolates
AUTHOR(S): Molitoris, D.; Vaisanen, M.-L.; Bolanos, M.; Finegold, S. M.
CORPORATE SOURCE: Research Services, VA Greater Los Angeles Healthcare System, UCLA School of Medicine, Los Angeles, CA, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(5), 1887-1889
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The activity of DX-619 was evaluated against 376 anaerobic isolates using the reference CLSI agar dilution method. Overall, 90% of the strains were susceptible to DX-619 at ≤1 μg/mL. It was more active than the other 4 compds. tested except for meropenem, which showed virtually identical overall activity.
IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparative in vitro antibiotic activity of DX-619 against anaerobic bacteria)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

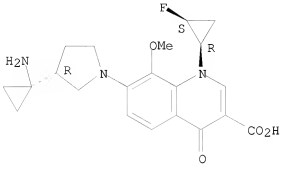
Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

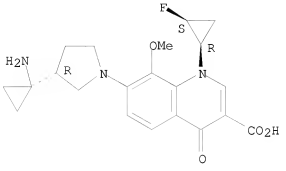
L3 ANSWER 21 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:343126 CA
TITLE: In vivo efficacies and pharmacokinetics of DX-619, a novel des-fluoro(6) quinolone, against Streptococcus pneumoniae in a mouse lung infection model. [Erratum to document cited in CA144:080646]
AUTHOR(S): Fukuda, Yuichi; Yanagihara, Katsunori; Ohno, Hideaki; Higashiyama, Yasuhito; Miyazaki, Yoshitsugu; Tsukamoto, Kazuhiro; Hirakata, Yoichi; Tomono, Kazunori; Mizuta, Yohei; Tashiro, Takayoshi; Kohno, Shigeru
CORPORATE SOURCE: Second Department of Internal Medicine and Department of Pharmacotherapeutics, Nagasaki University Graduate School of Pharmaceutical Sciences, Nagasaki, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(3), 1122
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 121, abstract, line 6, and on page 122, Results, line 9, "9.15" should read "9.71" . On page 122, Table 1, "ED50 (mg/kg/day) (95% confidence limits)" column, row 1 should read "9.711 (2.429 to 22.49)".
IT 431058-65-0, DX 619
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vivo efficacies and pharmacokinetics of DX-619 des-fluoro(6) quinolone against Streptococcus pneumoniae in mouse lung infection model (Erratum))
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 22 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:187906 CA
TITLE: In vitro activity of DX-619, a novel des-fluoro(6) quinolone, against a panel of Streptococcus pneumoniae mutants with characterized resistance mechanisms
AUTHOR(S): Wickman, Paul A.; Moland, Ellen Smith; Black, Jennifer A.; Thomson, Kenneth S.
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Center for Research in Anti-Infectives and Biotechnology, Creighton University School of Medicine, Omaha, NE, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(2), 796-798
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vitro activities of DX-619 and four other quinolones were compared against Streptococcus pneumoniae mutants that contained a variety of alterations within the quinolone resistance-determining regions. DX-619 was the most potent quinolone and was least affected by the mutations.
IT 431058-65-0, DX 619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro activity of fluoroquinolone antibiotic DX-619 against Streptococcus pneumoniae with characterized resistance mechanisms)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

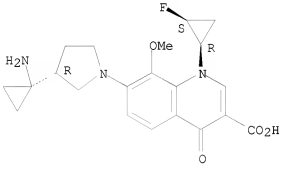
L3 ANSWER 23 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:187894 CA
TITLE: DX-619, a novel des-fluoro(6) quinolone manifesting low frequency of selection of resistant Staphylococcus aureus mutants: Quinolone resistance beyond modification of type II topoisomerases
AUTHOR(S): Strahilevitz, Jacob; Truong-Bolduc, Que Chi; Hooper, David C.
CORPORATE SOURCE: Division of Infectious Diseases, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(12), 5051-5057
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB DX-619, a novel des-fluoro(6) quinolone, was 16- to 32-fold, 2-fold, and 4- to 8-fold more potent than ciprofloxacin, gemifloxacin, and garenoxacin, resp., against wild-type S. aureus. DX-619 manifested equal 4-fold increases in MIC against a common parC mutant and a common gyrA mutant and selected for mutants at ≤2- to 4-fold its MIC, consistent with dual-targeting properties. Of the 4 independent single-step mutants selected, 2 had new single mutations in parC (V87F and R17H), and 2 shared a new gyrA mutation (A26V), 1 with an addnl. deletion mutation in parE (A215-7). By allelic exchange, the ParC but not the GyrA or ParE mutation was shown to be fully responsible for the resistance phenotypes, suggesting an as yet undefined mechanism of resistance operating in conjunction with type II topoisomerase mutations contributed to resistance to DX-619. Studies with purified topoisomerase IV and gyrase from S. aureus also showed that DX-619 had similar activity against topoisomerase IV and gyrase (50% stimulation of cleavage complexes concentration, 1.25 and 0.62 to 1.25 μg/mL, resp.). Susceptibility studies with DX-619 and an array of efflux pump substrates with and without reserpine, an inhibitor of efflux pumps, suggested that resistance in DX-619-selected mutants is affected by mechanisms other than mutations in topoisomerases or known reserpine-inhibitable pumps in S. aureus and thus are likely novel.

IT 431058-65-0, DX 619

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DX-619 is a novel des-fluoro(6) quinolone manifesting low frequency of selection of resistant Staphylococcus aureus mutants)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:141511 CA
TITLE: Recently approved and investigational antibiotics for treatment of severe infections caused by Gram-positive bacteria
AUTHOR(S): Appelbaum, Peter C.; Jacobs, Michael R.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Current Opinion in Microbiology (2005), 8(5), 510-517 CODEN: COMIF7; ISSN: 1369-5274
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The development of resistance in the major pathogenic Gram-pos. genera Staphylococcus and Streptococccus has led to the need for new agents that are able to overcome existing resistance mechanisms or that have novel mechanisms of action. There is currently a dearth of new agents that are active against resistant bacterial species. Agents that have recently been approved for clin. use include linezolid, the first oxazolidinone in clin. use, daptomycin, the first lipopeptide in clin. use, and telithromycin, a ketolide that is derived from clarithromycin. Agents currently in clin. development include tigecycline, a broad-spectrum i.v. tetracycline, ceftobiprole, a broad-spectrum cephalosporin that has activity against methicillin-resistant staphylococci, DX-619 and WCK-771, which are potent quinolones that have activity against quinolone-resistant staphylococci, oritavancin and dalbavancin, both of which are new glycopeptides, and iclaprim, which is a diaminopyrimidine. Addnl. agents that are in preclin. development against Gram-pos. pathogens include quinoline-naphthyridine agents, which target novel DNA gyrase sites, other novel quinolones that have high potency,

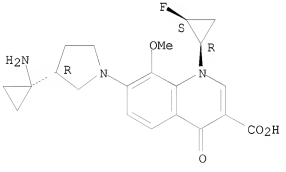
peptide deformylase inhibitors, and new lincosamide, oxazolidinone, lipopeptide and cephalosporin derivs. Misuse of potent new agents will, however, result in the inevitable development of resistance to these agents; responsible use of potent new agents is required to prevent continuation of this vicious cycle.

IT 431058-65-0, DX 619
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DX 619; DX-619 with activity against quinolone-resistant staphylococci might be useful for treatment for Gram pos. Staphylococcus, Streptococccus bacterial infection)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:94427 CA
TITLE: Quinolone-containing medicinal composition
INVENTOR(S): Yano, Emi; Kobayashi, Hideo; Kikuchi, Hiroshi; Yamaguchi, Yuri; Jindo, Toshimasa; Nishimoto, Norihiro
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006004028	A1	20060112	WO 2005-JP12177	20050701
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,				

ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005258398	A1	20060112	AU 2005-258398		20050701
CA 2572167	A1	20060112	CA 2005-2572167		20050701
EP 1764102	A1	20070321	EP 2005-755839		20050701
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR					
CN 1980670	A	20070613	CN 2005-80022507		20050701
MX 2007000336	A	20070328	MX 2007-336		20070108
KR 2007029280	A	20070313	KR 2007-702196		20070129
NO 2007000617	A	20070330	NO 2007-617		20070201
PRIORITY APPLN. INFO.:			JP 2004-197223	A	20040702
			WO 2005-JP12177	W	20050701

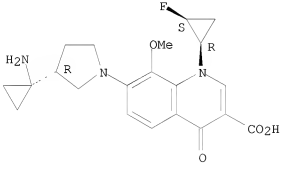
AB A liquid drug contains (1) 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylic acid or salts and hydrates thereof and (2) a compound of a polyvalent metal, at the molar ratio of the (2) to (1) being 0.01-0.7. A liquid drug for intravascular administration can be provided which contains the quinolone compound in a sufficient amount and which gives less trouble (e.g. precipitation), despite the incorporation of a small amount of the polyvalent metal compound, such as MgCl2. The compns. can be freeze-dried and diluents may comprise the polyvalent metal compds.

IT 431058-65-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(i.v. injections comprising quinolonecarboxylate and polyvalent metal compound)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:80646 CA

TITLE: In vivo efficacies and pharmacokinetics of DX-619, a novel des-fluoro(6) quinolone, against Streptococcus pneumoniae in a mouse lung infection model

AUTHOR(S): Fukuda, Yuichi; Yanagihara, Katsunori; Ohno, Hideaki; Higashiyama, Yasuhito; Miyazaki, Yoshitsugu; Tsukamoto, Kazuhiro; Hirakata, Yoichi; Tomono, Kazunori; Mizuta, Yohei; Tashiro, Takayoshi; Kohno, Shigeru

CORPORATE SOURCE: Second Department of Internal Medicine, Nagasaki University Graduate School of Pharmaceutical Sciences, Nagasaki, Japan

SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(1), 121-125
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

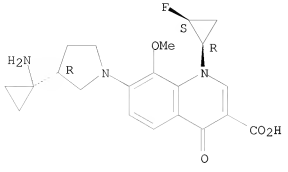
AB DX-619 is a novel des-fluoro(6) quinolone with potent activity against gram-pos. pathogens. The in vivo activity of DX-619 against Streptococcus pneumoniae was compared with those of fluoro(6) quinolones, sitafloxacin, and ciprofloxacin in a mouse model. Two strains of S. pneumoniae were used: a penicillin-sensitive S. pneumoniae (PSSP) strain and a penicillin-resistant S. pneumoniae (PRSP) strain. Furthermore, these strains showed intermediate susceptibilities to ciprofloxacin. In murine lung infections caused by PSSP, the 50% EDs (ED50s) of DX-619, sitafloxacin, and ciprofloxacin were 9.15, 11.1, and 127.6 mg/kg of body weight, resp. Against PRSP-mediated pneumonia in mice, the ED50s of DX-619, sitafloxacin, and ciprofloxacin were 0.69, 4.84, and 38.75 mg/kg, resp. The mean ± standard error of the mean viable bacterial counts in murine lungs infected with PSSP and treated with DX-619, sitafloxacin, ciprofloxacin (10 mg/kg twice daily), and saline (twice daily) were 1.75±0.06, 1.92±0.23, 6.48±0.28, and 7.57±0.13 log10 CFU/mL, resp. Furthermore, the nos. of viable bacteria in lungs infected with PRSP and treated with the three agents and not treated (control) were 1.73±0.04, 2.28±0.17, 4.61±0.59, and 5.54±0.72 log10 CFU/mL, resp. DX-619 and sitafloxacin significantly decreased the nos. of viable bacteria in the lungs compared to the nos. in the lungs of ciprofloxacin-treated and untreated mice. The pharmacokinetic parameter of the area under the concentration-time curve (AUC)/MIC ratio in the lungs for DX-619, sitafloxacin, and ciprofloxacin were 171.0, 21.92, and 1.22, resp. The AUC/MIC ratio in the lungs was significantly higher for DX-619 than for sitafloxacin and ciprofloxacin. Our results suggest that DX-619 and sitafloxacin are potent against both PSSP and PRSP in our mouse pneumonia model.

IT 431058-65-0, DX 619
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vivo efficacies and pharmacokinetics of DX-619, a des-fluoro(6) quinolone, against Streptococcus pneumoniae in a mouse lung infection model)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:23133 CA
TITLE: Preparation of peptides as bacterial efflux inhibitors and methods of treating bacterial infections
INVENTOR(S): Glinka, Tomasz; Bostian, Keith; Surber, Mark; Lomovskaya, Olga; Sun, Dongxu
PATENT ASSIGNEE(S): Mpex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113579	A1	20051201	WO 2005-US17841	20050520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005245962	A1	20051201	AU 2005-245962	20050520
CA 2571828	A1	20051201	CA 2005-2571828	20050520
EP 1758920	A1	20070307	EP 2005-751943	20050520
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008502720	T	20080131	JP 2007-527497	20050520
IN 2006DN07807	A	20070817	IN 2006-DN7807	20061221
PRIORITY APPLN. INFO.:			US 2004-574014P P	20040521
			WO 2005-US17841 W	20050520

OTHER SOURCE(S): CASREACT 144:23133; MARPAT 144:23133
AB The invention relates to the field of antimicrobial agents and more

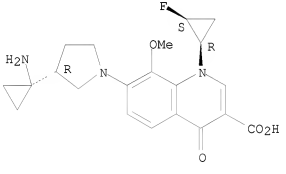
specifically it relates to efflux pump inhibitor (EPI) compds. to be co-administered with antimicrobial agents for the treatment of infections caused by drug resistant pathogens. The EPI compds. are soft drugs which exhibit a reduced propensity for tissue accumulation. The claims describes EPI peptides H-L-AA1-D-AA2-N(CG-1)CG-2 [AA1, AA2 are amino acid residues, CG-1 is H or a carbon-linked capping group, CG-2 is a carbon-linked capping group; CG-1 and CG-2 are optionally linked to form a 5- or 6-membered ring; any amino groups that are not part of an amide group are optionally acylated with an (S)-amino acid residue]. Thus, L-ornithyl-D-homophenylalanine quinoline-3-amide was prepared by amidation reactions and examined for stability in tissues and EPI activity.

IT 431058-65-0, DX 619
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed antimicrobial agent; preparation of peptides as bacterial efflux inhibitors and methods of treating bacterial infections)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 28 OF 40 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:435744 CA

TITLE: In vitro antibacterial activity of DX-619, a novel des-fluoro(6) quinolone. [Erratum to document cited in CA143:129882]

AUTHOR(S): Fujikawa, Katsuko; Chiba, Megumi; Tanaka, Mayumi; Sato, Kenichi

CORPORATE SOURCE: New Product Research Laboratories I, Daiichi Pharmaceutical Co. Ltd., Tokyo, Japan

SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(9), 3988
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

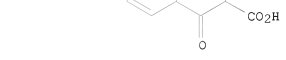
DOCUMENT TYPE: Journal

LANGUAGE: English

AB On page 3041, Table 1, right column, under "Streptococcus pneumoniae. Ciprofloxacin resistant," the entry "arenoxacin" should read "Garenoxin". On page 3042, Table 1, under "Enterococcus faecium. Vancomycin

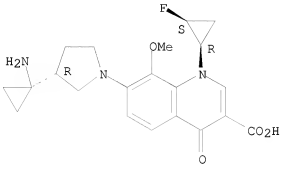
susceptible," the MIC range for gatifloxacin should be "0.25-64" and the MIC50 should be "8".
IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antibiotic activity of DX-619 des-fluoro(6) quinolone (Erratum))
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 29 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:435742 CA
TITLE: Postantibiotic effect of DX-619 against 16 Gram-positive organisms
AUTHOR(S): Pankuch, G. A.; Appelbaum, P. C.
CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(9), 3963-3965
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vitro postantibiotic effects (PAEs), the postantibiotic sub-MIC effects (PA-SMEs), and the sub-MIC effects (SMEs) of DX-619 were determined for 16 gram-pos. organisms. DX-619 pneumococcal, staphylococcal, and enterococcal PAE ranges were 1.7 to 5.0 h, 0.7 to 1.8 h, and 1.2 to 6.5 h, resp. The PA-SME ranges (0.4 + MIC) for pneumococci, staphylococci, and enterococci were 5.2 to >8.6 h, 2.1 to 8.3 h, and 4.9 to >10.0 h, resp.
IT 431058-65-0, DX 619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(postantibiotic effect of DX-619 against gram-pos. bacteria)
RN 431058-65-0 CA
CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:339598 CA
TITLE: Use and administration of bacterial efflux pump inhibitors
INVENTOR(S): Bostion, Keith; Glinka, Tomasz; Lomovskaya, Olga; Surber, Mark
PATENT ASSIGNEE(S): MPEX Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089738	A2	20050929	WO 2005-US8873	20050316
WO 2005089738	A3	20070823		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA				
CA 2559208	A1	20050929	CA 2005-2559208	20050316
EP 1732527	A2	20061220	EP 2005-732714	20050316
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
JP 2008500965	T	20080117	JP 2007-504097	20050316

PRIORITY APPLN. INFO.: US 2004-554143P P 20040317
US 2004-564916P P 20040422

WO 2005-US8873 W 20050316

OTHER SOURCE(S): MARPAT 143:339598

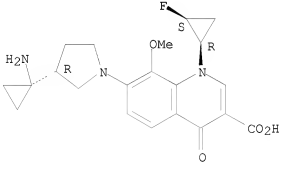
AB This invention provides for efflux pump inhibitors to be co-administered with antimicrobial agents for the treatment of infections caused by drug resistant pathogens, novel efflux pump inhibitors, combined dosage forms of efflux pump inhibitors with an antimicrobial, and novel medical methods.

IT 431058-65-0, DX 619
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use and administration of bacterial efflux pump inhibitors)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 31 OF 40 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:322100 CA

TITLE: Antistaphylococcal activity of DX-619, a new des-F(6)-quinolone, compared to those of other agents

AUTHOR(S): Bogdanovich, Tatiana; Esel, Duygu; Kelly, Linda M.; Bozdogan, Buelent; Credito, Kim; Lin, Gengrong; Smith, Kathy; Ednie, Lois M.; Hoellman, Dianne B.; Appelbaum, Peter C.

CORPORATE SOURCE: Department of Pathology, Hershey Medical Center, Hershey, PA, 17033, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(8), 3325-3333
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The in vitro activity of DX-619, a new des-F(6)-quinolone, was tested against staphylococci and compared to those of other antimicrobials. DX-619 had the lowest MIC ranges/MIC50s/MIC90s (μg/mL) against 131 Staphylococcus aureus strains (≤0.002 to 2.0/0.06/0.5) and 128 coagulase-neg. staphylococci (0.004 to 0.25/0.016/0.125). Among strains tested, 76 S. aureus strains and 51 coagulase-neg. staphylococci were resistant to ciprofloxacin. DX-619 had the lowest MIC50/MIC90 values against 127 quinolone-resistant staphylococci (0.125/0.5), followed by

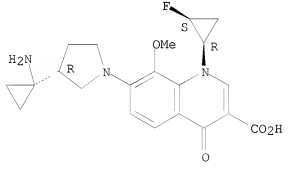
sitafloxacin (0.5/4), moxifloxacin (2/8), gatifloxacin (4/16), levofloxacin (16/>32), and ciprofloxacin (>32/>32). Raised quinolone MICs were associated with mutations in GyrA (S84L) and single or double mutations in GrlA (S80F or Y; E84K, G, or V) in all S. aureus strains tested. A recent vancomycin-resistant S. aureus (VRSA) strain (Hershey) was resistant to available quinolones and was inhibited by DX-619 at 0.25 μg/mL and sitafloxacin at 1.0 μg/mL. Vancomycin (except-VRSA), linezolid, ranbezolid, tigecycline, and quinupristin-dalfopristin were active against all strains, and teicoplanin was active against S. aureus but less active against coagulase-neg. staphylococci. DX-619 produced resistant mutants with MICs of 1 to >32 μg/mL after <50 days of selection compared to 16 to >32 μg/mL for ciprofloxacin, sitafloxacin, moxifloxacin, and gatifloxacin. DX-619 and sitafloxacin were also more active than other tested drugs against selected mutants and had the lowest mutation frequencies in single-step resistance selection. DX-619 and sitafloxacin were bactericidal against six quinolone-resistant (including the VRSA) and seven quinolone-susceptible strains tested, whereas gatifloxacin, moxifloxacin, levofloxacin, and ciprofloxacin were bactericidal against 11, 10, 7, and 5 strains at 4 + MIC after 24 h, resp. DX-619 was also bactericidal against one other VRSA strain, five vancomycin-intermediate S. aureus strains, and four vancomycin-intermediate coagulase-neg. staphylococci. Linezolid, ranbezolid, and tigecycline were bacteriostatic and quinupristin-dalfopristin, teicoplanin, and vancomycin were bactericidal against two, eight, and nine strains, and daptomycin and oritavancin were rapidly bactericidal against all strains, including the VRSA. DX-619 has potent in vitro activity against staphylococci, including methicillin-, ciprofloxacin-, and vancomycin-resistant strains.

IT 431058-65-0, DX 619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antistaphylococcal activity of des-F(6)-quinolone DX-619 compared with common antibiotics)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 32 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:172685 CA
TITLE: Preparation of rifamycin iminomethylenyl quinolone derivatives effective against drug-resistant microbes
INVENTOR(S): Ding, Charles Z.; Jin, Yafei; Longgood, Jamie C.; Ma, Zhenkun; Li, Jing; Kim, In Ho; Minor, Keith P.; Harran, Susan
PATENT ASSIGNEE(S): Cumbre Inc., USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070941	A1	20050804	WO 2005-US838	20050112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050209210	A1	20050922	US 2005-34279	20050112
US 7238694	B2	20070703		
EP 1723150	A1	20061122	EP 2005-705477	20050112
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-536018P P 20040113
WO 2005-US838 W 20050112
OTHER SOURCE(S): CASREACT 143:172685; MARPAT 143:172685
GI

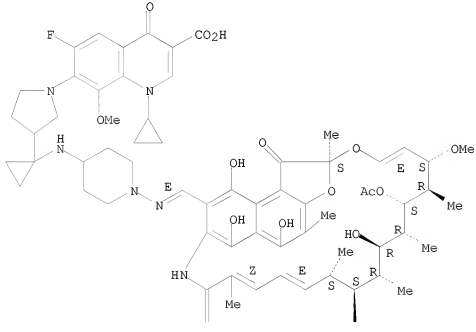
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Rifamycin 3-iminomethylenyl (-CH=N-) derivs. of formula I [A = quinolone group; X = alkylene, arylene, heterocyclylene, CO, C=N, O, etc.; R = H, acetyl, etc.] are prepared which have antimicrobial activities, including activities against drug-resistant microorganisms. The claimed rifamycin derivative has a rifamycin moiety covalently linked to a linker through an iminomethylenyl (-CH = N-) group at the C-3 carbon of the rifamycin moiety and the linker is, in turn, covalently linked to a quinolone structure or its pharmacophore within the DNA gyrase and topoisomerase IV inhibitor family. The inventive rifamycins are novel and exhibit activity against both rifampin and ciprofloxacin-resistant microorganisms. Thus, II was prepared from ciprofloxacin and 3-formylrifamycin SV. The prepared compds. have MIC values of 0.06-16 mcg/mL against Staphylococcus aureus ATCC 29213 RpoBH418Y.

IT 861391-37-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of rifamycin iminomethylene quinolone derivs. as antimicrobial agents)
RN 861391-37-9 CA
CN Rifamycin, 3-[(E)-[[4-[[1-[1-(3-carboxy-1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-4-oxo-7-quinolinyl)-3-pyrrolidinyl]cyclopropyl]amino]-1-piperidinyl]imino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 33 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:129882 CA
TITLE: In vitro antibacterial activity of DX-619, a novel des-fluoro(6) quinolone
AUTHOR(S): Fujikawa, Katsuko; Chiba, Megumi; Tanaka, Mayumi; Sato, Kenichi

CORPORATE SOURCE: New Product Research Laboratories I, Daiichi Pharmaceutical Co. Ltd., Tokyo, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(7), 3040-3045
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

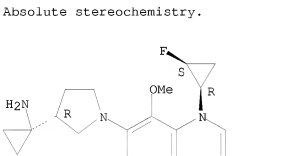
AB The in vitro activities of DX-619, des-fluoro(6) quinolone, against 1,208 clin. isolates were examined DX-619 was particularly potent against staphylococci, including ciprofloxacin- and methicillin-resistant strains; the MIC at which 90% of the strains tested were inhibited was 0.5 μg/mL. In addition, DX-619 was also active against gram-neg. bacteria.

IT 431058-65-0, DX-619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antibiotic activity of DX-619 des-fluoro(6) quinolone)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

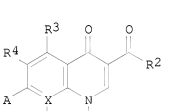
L3 ANSWER 34 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:26640 CA
TITLE: Preparation of quinolone antibacterial agents
INVENTOR(S): Ellsworth, Edmund Lee; Taylor, Clarke Bentley; Murphy, Sean Timothy; Rauckhorst, Mark Ryan; Starr, Jeremy Tyson; Hutchings, Kim Marie; Limberakis, Chris; Hoyer, Denton Wade
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005049602	A1	20050602	WO 2004-IB3666	20041105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NL 1027545	C2	20060117	NL 2004-1027545	20041118
PRIORITY APPLN. INFO.:			US 2003-523071P	P 20031118
			US 2004-605496P	P 20040831

OTHER SOURCE(S): MARPAT 143:26640

GI



I

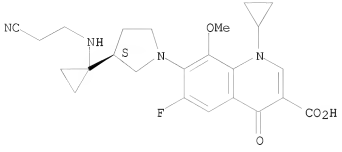
AB Compds. of formula I, e.g., 7-[3-(2-Cyanoethylamino)pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, can be used in a variety of applications including use as antibacterial agents. The compds., method of treatment using the compds., and formulations containing the compds. are claimed. Methods of preparation of the compds. are exemplified. The compds. of the invention were tested against a variety of gram-neg. and gram-pos. organisms.

IT 852857-63-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of quinolone antibacterial agents)

RN 852857-63-7 CA

CN 3-Quinolinecarboxylic acid, 7-[(3S)-3-[1-[(2-cyanoethyl)amino]cyclopropyl]-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



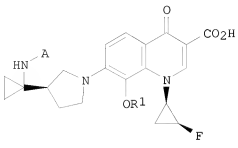
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 35 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:93693 CA
TITLE: Process for preparation of quinolinone derivatives
INVENTOR(S): Muto, Makoto; Kitagawa, Yutaka
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113321	A1	20041229	WO 2004-JP8607	20040618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1634879	A1	20060315	EP 2004-746109	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 20060122396	A1	20060608	US 2005-560823	20051215

PRIORITY APPLN. INFO.: JP 2003-175212 A 20030619
WO 2004-JP8607 W 20040618

OTHER SOURCE(S): MARPAT 142:93693
GI



I

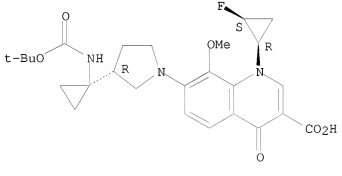
AB This invention pertains to a method for position-selectively introducing an amino group into a difluorobenzoic acid compound; a novel process for producing quinolinone derivs. I [wherein A = a protecting group; R1 = alkyl]. For example, the compound I [where A = tert-BuO2C; R1 = Me] was prepared in a multi-step synthesis starting from 2,4-difluoro-3-methoxybenzoic acid and (3R)-3-[1-(tert-butoxycarbonylamino)cyclopropyl]pyrrolidine. This invention provides a convenient method for regioselective amination of difluorobenzoic acid compound

IT 817194-48-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinolinone derivs. via regioselective amination)

RN 817194-48-2 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-[1-[[(1,1-dimethylethoxy)carbonyl]amino]cyclopropyl]-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

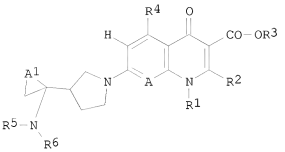
L3 ANSWER 36 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 136:401768 CA
TITLE: Preparation of dehalogenoquinolinecarboxylic acid derivatives, naphthyridine derivatives, and benzoxazine derivatives as antibacterial agents
INVENTOR(S): Takahashi, Hisashi; Miyauchi, Rie; Itoh, Masao;

Takemura, Makoto; Hayakawa, Isao
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040478	A1	20020523	WO 2001-JP10086	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429440	A1	20020523	CA 2001-2429440	20011119
AU 2002024050	A	20020527	AU 2002-24050	20011119
EP 1336611	A1	20030820	EP 2001-996540	20011119
EP 1336611	B1	20070905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015326	A	20040225	BR 2001-15326	20011119
JP 3711108	B2	20051026	JP 2002-543488	20011119
CN 1269817	C	20060816	CN 2001-822074	20011119
RU 2298006	C2	20070427	RU 2003-114743	20011119
AT 372338	T	20070915	AT 2001-996540	20011119
ES 2292642	T3	20080316	ES 2001-996540	20011119
IN 2003CN00734	A	20050415	IN 2003-CN734	20030514
NO 2003002255	A	20030721	NO 2003-2255	20030519
NO 326157	B1	20081013		
US 20040063754	A1	20040401	US 2003-432043	20030519
ZA 2003003871	A	20040819	ZA 2003-3871	20030519
MX 2003PA04437	A	20040504	MX 2003-PA4437	20030520
KR 777149	B1	20071119	KR 2003-706835	20030520
HK 1056729	A1	20080206	HK 2003-109128	20031215
JP 2004269544	A	20040930	JP 2004-156517	20040526
JP 2005194274	A	20050721	JP 2004-379455	20041228
JP 3760172	B2	20060329		
US 20070123560	A1	20070531	US 2006-644901	20061226

PRIORITY APPLN. INFO.:			
JP 2000-352269	A	20001120	
JP 2001-248822	A	20010820	
JP 2002-543488	A3	20011119	
WO 2001-JP10086	W	20011119	
US 2003-432043	A1	20030519	

OTHER SOURCE(S): MARPAT 136:401768
GI



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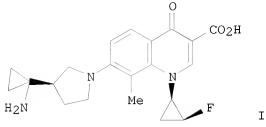


II

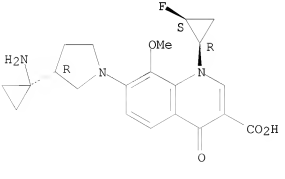
AB The title compds. I [R1 = alkyl, etc.; R2 = alkylthio, H; further detail on R1 and R2 is given; R3 = H, Ph, etc.; R4 = alkyl, etc.; A = N, etc.; R5, R6 = alkyl, etc.; A1 = (CH2)n; n = 1 or 2] are prepared I exhibit broad and potent activity against gram-neg. and gram-pos. bacteria and against resistant bacteria. The title compound II in vitro showed MIC of 0.025 μg/mL against P. aeruginosa 32121. Formulations are given.

IT 431058-65-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dehalogenoquinolinecarboxylic acid derivs., naphthyridine derivs., and benzoxazine derivs. as antibacterial agents)

RN 431058-65-0 CA

CN 3-Quinolinecarboxylic acid, 7-[(3R)-3-(1-aminocyclopropyl)-1-pyrrolidinyl]-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.

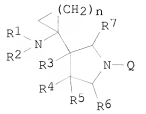


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 37 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 133:237871 CA
TITLE: Preparation of cis-substituted aminocycloalkylpyrrolidine derivatives of 1,4-dihydro-4-oxoquinoline-3-carboxylic acids as antimicrobial drugs
INVENTOR(S): Takemura, Makoto; Kimura, Youichi; Takahashi, Hisashi; Kimura, Kenichi; Miyauchi, Satoru; Ohki, Hitoshi; Sugita, Kazuyuki; Miyauchi, Rie
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 67 pp., Cont.-in-part of Appl. No. PCT/JP96/03440.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6121285	A	20000919	US 1998-82155	19980521
WO 9719072	A1	19970529	WO 1996-JP3440	19961122
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9804273	A	19981125	ZA 1998-4273	19980520
US 6184388	B1	20010206	US 1999-397515	19990917
PRIORITY APPLN. INFO.:			JP 1995-304129	A 19951122
			JP 1996-192637	A 19960723
			WO 1996-JP3440	A2 19961122
			JP 1997-131413	A 19970521
			JP 1997-140643	A 19970529
			US 1998-82155	A1 19980521

OTHER SOURCE(S): MARPAT 133:237871
GI



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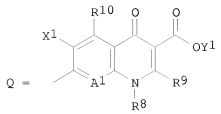
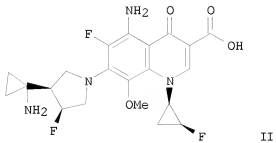




II

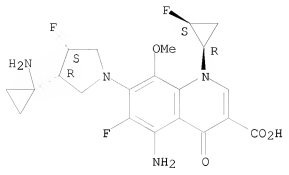
AB The title compds. (I) [wherein R1, R6, and R7 = independently H or alkyl; R2 = H or (un)substituted alkyl; R3 = H, OH, halo, carbamoyl, alkyl, alkoxy, or alkylthio; one of R4 and R5 = H and the other is CH2OH, Me, OMe, or F; or R4 and R5 together = hydroxyimino, a polymethylene chain of 3-6 C's which form a spirocyclic structure together with the pyrrolidine ring or an alkoxyimino group; n = 1-3; R8 = (halo)alkyl, alkenyl, alkoxy, alkylamino, (un)substituted cycloalkyl or (hetero)aryl, etc.; R9 = H or alkylthio; X1 = H or halo; R10 = H, NH2, OH, SH, halomethyl, alkyl, alkenyl, or alkoxy; A1 = N or (un)substituted C; Y1 = H, Ph, acetoxymethyl, pivaloyloxymethyl, ethoxycarbonyl, etc.] were prepared I have excellent antimicrobial activity and are highly safe. Thus, 1-benzyloxycarbonyl-4-(R)-(1-tert-butoxycarbonylaminocyclopropyl)-3-(S)-fluoropyrrolidine was dissolved in EtOH and hydrogenated using Pd/C. A solution of the residue and DMSO was mixed with TEA and 5-amino-6,7-difluoro-1-[2-(S)-fluoro-1-(R)-cyclopropyl]-1,4-dihydro-8-methoxy-4-oxoquinoline-3-carboxylic acid to give II (43%). II was tested on 13 microbial strains and showed potent inhibition with MIC values ranging from ≤ 0.003 μg/mL to 0.39 μg/mL. In an acute toxicity test on male mice, none of the five mice died upon administration of 150 mg/kg doses of II.

IT 190954-09-7P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-(aminocycloalkylpyrrolidinyl)-1,4-dihydro-4-oxoquinolines as antimicrobial agents by addition of 6-fluoro-1,4-dihydro-4-oxoquinolines to aminocycloalkylpyrrolidines)

RN 190954-09-7 CA

CN 3-Quinolinecarboxylic acid, 5-amino-7-[(3R,4S)-3-(1-aminocyclopropyl)-4-fluoro-1-pyrrolidinyl]-6-fluoro-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



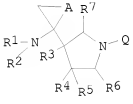
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 38 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 130:13992 CA
TITLE: Preparation and formulation of cis-disubstituted aminocycloalkylpyrrolidine moiety-containing quinoline and benzoxazine derivatives as bactericides
INVENTOR(S): Takemura, Makoto; Takahashi, Hisashi; Sugita, Kazuyuki; Ohki, Hitoshi; Miyauchi, Satoru; Miyauchi, Rie
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9852939	A1	19981126	WO 1998-JP2219	19980520
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9804273	A	19981125	ZA 1998-4273	19980520
CA 2289605	A1	19981126	CA 1998-2289605	19980520
AU 9874493	A	19981211	AU 1998-74493	19980520
EP 1020459	A1	20000719	EP 1998-921738	19980520
EP 1020459	B1	20050406		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9810235	A	20010918	BR 1998-10235	19980520
IN 1998MA01076	A	20050304	IN 1998-MA1076	19980520
AT 292632	T	20050415	AT 1998-921738	19980520
NO 9905653	A	20000121	NO 1999-5653	19991118
MX 9910715	A	20000831	MX 1999-10715	19991119

US 20020077345 A1 20020620 US 2001-985256 20011102
PRIORITY APPLN. INFO.: JP 1997-131413 A 19970521
JP 1997-140643 A 19970529
WO 1998-JP2219 W 19980520
US 1999-424112 A1 19991119

OTHER SOURCE(S): MARPAT 130:13992
GI



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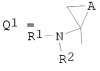
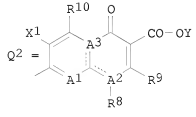




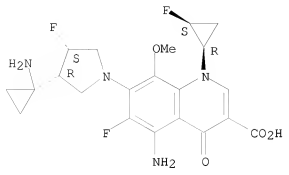
AB The title compds. I [R1 represents hydrogen or alkyl; R2 represents hydrogen or alkyl; R3 and R5 represent each hydrogen; R4 represents hydroxy, halogeno, carbamoyl, alkyl, alkoxy or alkylthio; R6 and R7 represent each hydrogen or alkyl; A = (CH2)n; n is an integer of from 1 to 3; R4 and the substituent on the pyrrolidine ring of general formula Q1 are arranged at the cis-configuration; and Q is a partial structure represented by Q2; R8 = alkyl, etc.; R9 = H, etc.; further details on R9 and R8 are given; R10 = amino, etc.; X1 = halo, H; A1 = N, etc.; A2, A3 = N, C; further details on A2 and A3 are given; Y = H, etc.] are prepared Three compds. of this invention in vitro showed MIC values of 0.10 to 0.39 μg/mL against P. aeruginosa 32104.

IT 190954-09-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cis-disubstituted aminocycloalkylpyrrolidine moiety-containing
quinoline and benzoxazine derivs. as bactericides)

RN 190954-09-7 CA

CN 3-Quinolinecarboxylic acid, 5-amino-7-[(3R,4S)-3-(1-aminocyclopropyl)-4-fluoro-1-pyrrolidinyl]-6-fluoro-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

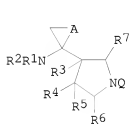
L3 ANSWER 39 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 127:50550 CA
ORIGINAL REFERENCE NO.: 127:9645a,9648a
TITLE: Preparation and formulation of substituted aminocycloalkylpyrrolidinylquinolines as medical bactericides
INVENTOR(S): Takemura, Makoto; Kimura, Youichi; Takahashi, Hisashi; Kimura, Kenichi; Miyauchi, Satoru; Ohki, Hitoshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719072	A1	19970529	WO 1996-JP3440	19961122
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2238765	A1	19970529	CA 1996-2238765	19961122
AU 9675898	A	19970611	AU 1996-75898	19961122
AU 707889	B2	19990722		
CN 1207738	A	19990210	CN 1996-199713	19961122
CN 1119343	C	20030827		
EP 911328	A1	19990428	EP 1996-938533	19961122
EP 911328	B1	20060208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 322202	A	20000526	NZ 1996-322202	19961122
TW 402601	B	20000821	TW 1996-85114493	19961122
AT 317393	T	20060215	AT 1996-938533	19961122
PT 911328	T	20060531	PT 1996-938533	19961122
ES 2258780	T3	20060901	ES 1996-938533	19961122

JP 4040091	B2	20080130	JP 1997-519602		19961122
NO 9802297	A	19980722	NO 1998-2297		19980520
US 6121285	A	20000919	US 1998-82155		19980521
US 6184388	B1	20010206	US 1999-397515		19990917
PRIORITY APPLN. INFO.:			JP 1995-304129	A	19951122
			JP 1996-192637	A	19960723
			WO 1996-JP3440	W	19961122
			JP 1997-131413	A	19970521
			JP 1997-140643	A	19970529
			US 1998-82155	A1	19980521

OTHER SOURCE(S): MARPAT 127:50550

GI



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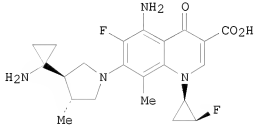


II

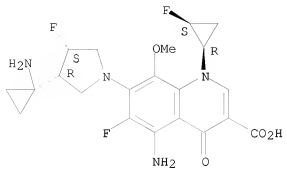
AB The title compds. I [R1 = H, alkyl; R2 = H, (un)substituted alkyl; R3 = H, halo, etc.; R4, R5 = H, OH, etc.; further details on R4, R5 are given; R6, R7 = H, alkyl; A = (CH2)n; n = 1 - 3; Q = quinoline moiety or analog (generic structures given)] are prepared The title compound II (preparation given)
in vitro showed MIC of 0.1 μg/mL against Pseudomonas aeruginosa 32121.

IT 190954-09-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted aminocycloalkylpyrrolidinylquinolines as medical bactericides)

RN 190954-09-7 CA

CN 3-Quinolinecarboxylic acid, 5-amino-7-[(3R,4S)-3-(1-aminocyclopropyl)-4-fluoro-1-pyrrolidinyl]-6-fluoro-1-[(1R,2S)-2-fluorocyclopropyl]-1,4-dihydro-8-methoxy-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 40 OF 40 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 125:247632 CA
ORIGINAL REFERENCE NO.: 125:46285a,46288a
TITLE: Preparation and formulation of heterocyclic compounds as medical bactericides
INVENTOR(S): Takemura, Makoto; Kimura, Youichi; Kawakami, Katsuhiro; Kimura, Kenichi; Ohki, Hitoshi; Matsuhashi, Norikazu; Kawato, Haruko
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

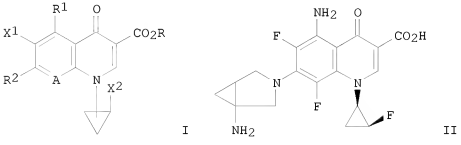
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623782	A1	19960808	WO 1996-JP208	19960201
W: CA, CN, FI, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2212007	A1	19960808	CA 1996-2212007	19960201
CA 2212007	C	20040914		
JP 08277284	A	19961022	JP 1996-16260	19960201
JP 3745433	B2	20060215		
EP 807630	A1	19971119	EP 1996-901518	19960201
EP 807630	B1	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
TW 487701	B	20020521	TW 1996-85101378	19960201
EP 1304329	A2	20030423	EP 2003-883	19960201
EP 1304329	A3	20040915		
EP 1304329	B1	20081015		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 239720	T	20030515	AT 1996-901518	19960201
PT 807630	T	20030829	PT 1996-901518	19960201
ES 2198474	T3	20040201	ES 1996-901518	19960201
AT 411309	T	20081015	AT 2003-883	19960201
NO 9703530	A	19971002	NO 1997-3530	19970731
NO 314546	B1	20030407		
FI 9703207	A	19971001	FI 1997-3207	19970801
US 5849757	A	19981215	US 1997-875678	19970804

PRIORITY APPLN. INFO.:

JP 1995-15614	A	19950202
JP 1995-19478	A	19950207
JP 1995-19481	A	19950207
EP 1996-901518	A3	19960201
WO 1996-JP208	W	19960201

OTHER SOURCE(S): MARPAT 125:247632

GI



I II

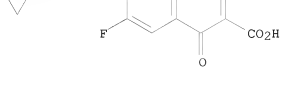
AB The title compds. I [X1 represents halo or hydrogen; X2 represents halo; R1 represents hydrogen, hydroxy, thiol, halomethyl, amino, alkyl or alkoxy; R2 represents a pyrrolidine moiety (generic structure given); A represents nitrogen, etc.; and R represents hydrogen, Ph, acetoxymethyl, pivaloyloxymethyl, ethoxycarbonyl, choline, dimethylaminoethyl, 5-indanyl, etc.] are prepared The title compound II (preparation given) in vitro showed MIC values of ≤ 0.003 μg/mL and 0.05 μg/mL against E. coli NIHJ and P. aeruginosa 32104, resp.

IT 181941-18-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as medical bactericides)

RN 181941-18-4 CA

CN 3-Quinolinecarboxylic acid, 7-[3-(1-aminocyclopropyl)-1-pyrrolidinyl]-6-fluoro-1-(2-fluorocyclopropyl)-1,4-dihydro-8-methoxy-4-oxo-, [1R-[1α(R*),2α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/560,823 final compound

=>

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Executing the logoff script...

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STN INTERNATIONAL LOGOFF AT 10:14:50 ON 22 JAN 2009